

USE OF DERIVATIVES OF CHITIN SOLUBLE IN AQUEOUS SOLUTIONS FOR PREVENTING ADHESIONS

This is a continuation of application Ser. No. 429,687, filed on Oct. 31, 1989, now abandoned.

FIELD OF THE INVENTION

This invention relates to an adhesion preventive. More particularly it relates to a biocompatible material which is useful in surgical operations for preventing adhesions of vital tissues such as skin, blood vessels or organs.

DESCRIPTION OF THE PRIOR ART

Vital tissues such as blood vessels or organs including kidney, liver and intestines are coated with mucous membranes or serous membranes so that they can function independently of each other. Examples of these mucous or serous membranes are the body wall pleura and organ pleura in the thoracic cavity and the parietal peritoneum and mesentery in the abdominal cavity, each protecting the corresponding organs. Surgical operations or inflammation in those portions of the body coated with serous membranes could result in adhesion regardless of the size of the affected part. Such adhesion between vital tissues may be observed not only in particular portions of the body but in all vital tissues. Adhesion between vital tissues has heretofore presented a serious problem in the surgical field.

In the field of orthopedics, conditions such as acute or chronic arthritis such as suppurative, rheumatoid arthritis, gonorrheal, tuberculous or traumatic injuries at a joint, such as fracture or sprain, would result in ankylotic diseases wherein the surface of the bones constituting the joint adhere to each other and thereby restrict the mobility of the joint. Congenital radioulnar synostosis wherein a spoke bone and an ulna adhere together is difficult to remedy by a surgical operation, since the separated bones would frequently re-adhere.

As described above, adhesion of vital tissues, large or small, may be observed in most surgical fields. Adhesion could occur for various reasons including mechanical and chemical stimulations of vital tissues accompanying surgical operations, postoperative bacterial infection, inflammation or complications. Consequently, it is necessary to prevent postoperative adhesion between vital tissues.

Conventional adhesion preventives such as liquid paraffin, camphor oil, chondroitin sulfate and urea exhibit an insufficient effect since they function only temporarily. On the other hand, synthetic polymer membranes such as gutta percha or poly(tetrafluoroethylene), which have been used for preventing postoperative adhesion at portions of the body where there is a fear of adhesion setting in, would remain in the body as foreign bodies. Therefore, it is necessary to take out the used membrane by reoperation.

Consequently, there has been a long felt need to find ways to prevent adhesions after surgery. Others have addressed the problem of adhesion prevention utilizing biodegradable materials. U.S. Pat. No. 4,603,695 which issued on Aug. 5, 1986 to Ikada et al refers to the use of an absorbable polyester polymer. This patent also mentions, in passing, the use of chitin. This material can be absorbed by hydrolysis in vivo.

Chitin and chitosan (partially deacetylated chitin) are well known biocompatible materials whose preparation has been described in U.S. Pat. No. 2,040,880 which issued on May 19, 1936. A derivative of chitosan, N,O-carboxymethyl chitosan, and its production has been described in U.S. Pat. No. 4,619,995 which issued on Oct. 28, 1986 to E.R. Hayes.

Uses of chitin and other polysaccharides for wound healing or adhesion prevention purposes are referred to in U.S. Pat. Nos. 3,632,754, 4,532,134, 4,659,700, 4,572,906, 4,378,017, British Patent 2026516, European Patent 200574 and PCT publications WO 86/00912, WO 87/07618 (PCT/US87/01246). None of these patents or publications, however, teach a simple way of forming films and gels from derivatives of chitin which are soluble in aqueous solutions.

SUMMARY OF THE INVENTION

It is an object of this invention to provide a biodegradable, absorbable material capable of preventing adhesions.

It is another object of this invention to provide a material for prevention of adhesions which can form a visco-elastic fluid by temporarily being cross-linked by non-toxic ionic bridges which will begin to degrade after a predetermined time period.

It is yet an additional object of the invention to provide a material for preventing adhesions which can be made from biocompatible material which can be easily made into a flexible film, a gel or a membrane having a gel core and can be easily and safely applied during surgery performed on humans or other mammals.

Accordingly, these and related objects are achieved by a preferred method which includes placing a material comprising biodegradable derivatives of chitin, which are soluble in dilute acidic aqueous solutions, between the tissues in order to prevent adhesions.

One adhesion prevention material of the present invention is an aqueous hydrogel polymer which dissolves over time in vital tissues. Since this material already contains water in order to obtain the desired properties, later hydrolysis is unnecessary. In the past, hydrogels have been used but they have either been covalently cross-linked to improve their life, and therefore have undesirably long degradation times, or else they did not last long enough in the site to be effective. The adhesion prophylaxis of the present invention comprises a polymer which is biocompatible and biodegradable comprised of polysaccharide units which may be broken down by the body into simple sugars which are then metabolized. The half life of the hydrogel material to be used in adhesion prevention can range from about 2-3 days to up to about one year in vivo. Therefore, it is possible to prevent adhesion by placing the adhesion preventative at that portion of the body of a warm blooded mammal undergoing surgery where there is a fear of adhesion setting in. The period the prophylaxis stays in place depends on the rate of absorption by dissolution or by degradation. The adhesion preventative made of the material of the present invention will disappear without requiring reoperation for its removal.

In one preferred embodiment the derivative of chitin is N,O CM-chitosan, and a second preferred derivative of chitin is chitosan. Other preferred derivatives of chitin are N, CM-chitosan; O, CM-chitosan; sulfated N, CM-chitosan and CM-chitin.

The preferred method may further comprise the step of forming a gel prior to placing the material between